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Abstract

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Grant Number: 5R01NR003915-09

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PI Title: ASSOCIATE PROFESSOR

Project Title: PERIOPERATIVE PAIN, IMMUNE FUNCTION, AND METASTASIS

Abstract: *DESCRIPTION (Adapted from the Investigator's Abstract): Pain management is an important aspect of the nursing care of individuals recovering from surgery. Painful stress such as surgery can suppress immune function and promote metastasis. In rats, the pre- and post- operative administration of morphine was shown to ameliorate the metastatic-enhancing effects of surgery. The overall objective of this research is to explore the mechanisms by which the pain of undergoing and recovering from surgery suppresses immune function and increases metastasis. Using a rat model, drug interventions are used to provide a means by which to assess the specific role of local, peripheral, and central pain mechanisms as well as neuroendocrine involvement in the immune and metastasis consequences of surgery. Proposed interventions include: (1) opiates to address central pain mechanisms; (2) non-steroidal anti-inflammatory drugs to block prostaglandin production resulting from tissue injury; (3) local neural blockade to block nociceptive impulse transmission at the injury site; (4) regional neural blockade to block nociceptive impulse transmission at the spinal cord; (5) an N-methyl-D-aspartate receptor antagonist to block the central facilitation of afferent impulses; (6) anxiolytics to reduce the stressful nature of surgery; and, (7) glucocorticoid receptor blockade and beta-adrenergic blockade to block specific interactions between the neuroendocrine and immune systems. Given previous findings of sex hormone-related differences in responses to both stress and drugs affecting pain processes, both female and male rats are used. Fischer 344 males and females in proestrus/estrus and metestrus/diestrus undergo either a standard laparotomy and anesthesia or anesthesia only and receive either the intervention or vehicle. Outcome measures include natural killer (NK) cell activity, the seeding of NK-sensitive tumor cells*

in the lungs, and two indicators of neuroendocrine activity: serum corticosterone and beta-endorphin levels. Given its NK sensitivity and syngeneity to the inbred Fischer 344 rat, the MADB106 tumor model is consistent with what is known about metastasis in humans. The findings of the proposed study have the potential to provide compelling evidence that it is the pain of undergoing and recovering from surgery that mediates the life-threatening immunosuppressive and metastatic-enhancing sequelae of surgery.

Thesaurus Terms:
analgesic, immunity, immunosuppression, metastasis, opioid, pain, postoperative state NMDA receptor, cancer prevention, corticosteroid receptor, disease /disorder model, drug screening /evaluation, hypothalamic pituitary adrenal axis, natural killer cell, neural facilitation, neural transmission, postoperative complication, preoperative state laboratory rat, neoplastic cell

Institution:	JOHNS HOPKINS UNIVERSITY 3400 N CHARLES ST BALTIMORE, MD 21218
Fiscal Year:	2001
Department:	NONE
Project Start:	30-SEP-1994
Project End:	30-APR-2002
ICD:	NATIONAL INSTITUTE OF NURSING RESEARCH
IRG:	NURS